

Appl. No. 10/660,206

Preliminary Amendment dated April 23, 2004

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1-24. (canceled)

25. (original) A conjugate peptide or polypeptide formed from two or more amino acid sequences that comprise:

- (a) one or more amino acid sequences that are capable of forming a stable coiled-coil solution structure corresponding to or mimicking the heptad repeat region of gp41 (N-helical domain); and
- (b) one or more amino acid sequences that correspond to, or mimic, an amino acid sequence of the transmembrane-proximal amphipathic α -helical segment of gp41 (C-helical domain);

wherein

said one or more sequences (a) and (b) are alternately linked to one another via a bond, such as a peptide bond (amide linkage) or by an amino acid linking sequence consisting of about 2 to about 25 amino acids.

26. (original) The conjugate of claim 25, wherein:

said N-helical peptide comprises about 28 to 55 amino acids of the following sequence:

ARQLLSGIVQQQNNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQQLLGI
(SEQ. ID NO: 1), or multimers thereof; and

said C-helical peptide comprises about 24-56 amino acids of the following sequence:

WNNMTWMEWDREINNYTSLIHSLIEESQNQQEKNEQELLELDKWASLWNWFNI
TNW (SEQ ID NO:4), or multimers thereof.

27. (original) The conjugate of claim 25, wherein:

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said N-helical peptide is one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, or one of SEQ ID NO: 9 through SEQ ID NO: 40, and wherein the peptide can be optionally coupled to a larger carrier protein, or optionally include a terminal protecting group at the N- and/or C- termini; and

said C-helical peptide is one of SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, or one of SEQ ID NO: 41 through SEQ ID NO: 74, and wherein the peptide can be optionally coupled to a larger carrier protein, or optionally include a terminal protecting group at the N- and/or C- termini.

28. (original) A pharmaceutical composition comprising a conjugate of claim 25, and a pharmaceutical acceptable carrier.

29. (original) A composition comprising polyclonal or monoclonal antibodies that are raised to the conjugate of claim 25.

30. (original) A composition comprising a mixture of C-helical peptide or polypeptide and N-helical peptide or polypeptide, wherein said mixture forms a stable core helix solution structure.

31. (original) The composition of claim 30, wherein:

said N-helical peptide comprises about 28 to 55 amino acids of the following sequence:

ARQLLSGIVQQQNNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQQLLGI
(SEQ. ID NO: 1), or multimers thereof; and

said C-helical peptide comprises about 24-56 amino acids of the following sequence:

WNNMTWMEWDREINNYTSLIHSLIEESQNQQEKNEQELLELDKWASLWNWFNI
TNW (SEQ ID NO:4), or multimers thereof.

32. (original) The composition of claim 30, wherein:

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said N-helical peptide is one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, or one of SEQ ID NO: 9 through SEQ ID NO: 40, and wherein the peptide can be optionally coupled to a larger carrier protein, or optionally include a terminal protecting group at the N- and/or C- termini; and

said C-helical peptide is one of SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, or one of SEQ ID NO: 41 through SEQ ID NO: 74, and wherein the peptide can be optionally coupled to a larger carrier protein, or optionally include a terminal protecting group at the N- and/or C- termini.

33. (original) A composition comprising polyclonal or monoclonal antibodies that are raised to the composition of claim 30.

34. (original) A method of treatment, comprising:
administering to an individual a composition comprising polyclonal or monoclonal antibodies as claimed in claim 29 or claim 33 in an amount effective to reduce HIV infection of uninfected cells.

35. (original) An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence encoding a peptide or polypeptide conjugate of claim 25.

36. (original) The nucleic acid molecule of claim 35, wherein said polynucleotide has the nucleotide sequence in FIG. 7.

37. (original) A method for making a recombinant vector comprising inserting an isolated nucleic acid molecule of claim 35 into a vector.

38. (original) A recombinant vector produced by the method of claim 37.

39. (original) A method of making a recombinant host cell comprising

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introducing the recombinant vector of claim 38 into a host cell.

40. (original) A recombinant host cell produced by the method of claim 39.

41. (original) A recombinant method for producing a conjugate peptide or polypeptide, comprising culturing the recombinant host cell of claim 40 under conditions such that said polypeptide is expressed and recovering said polypeptide.

42. (original) The method of claim 1, claim 8, claim 15 or claim 20, wherein said administering is provided in advance of any symptoms of HIV infection, or in advance of any known exposure to HIV.

43. (original) The method of claim 1, claim 8, claim 15 or claim 20, wherein said administering is provided upon or after the detection of symptoms which indicate that an animal may be infected with HIV, or upon or after exposure to the virus.

44. (new) A method of raising a broadly neutralizing antibody response to HIV comprising:

administering to a mammal a peptide or polypeptide wherein said peptide or polypeptide comprises:

- i) SEQ ID NO:2, SEQ ID NO:3, or one of SEQ ID NO:9 through SEQ ID NO: 40; or
- ii) a peptide having 1 to 10 conservative amino acid substitutions of SEQ ID NO:2, SEQ ID NO:3, or one of SEQ ID NO:9 through SEQ ID NO:40.

45. (new) The method of claim 44, wherein said peptide or polypeptide is coupled to a terminal protecting group at the N- and/or C-termini.

46. (new) The method of claim 44, wherein said peptide or polypeptide comprises SEQ ID NO:2 or SEQ ID NO:3.

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47. (new) The method of claim 44, wherein said peptide or polypeptide is conjugated to a carrier protein.

48. (new) The method of claim 47, wherein said carrier protein is keyhole limpet hemocyanin (KLH), ovalbumin, bovine serum albumin (BSA) or tetanus toxoid.

49. (new) A method of raising a broadly neutralizing antibody response to HIV comprising:
administering to a mammal a peptide or polypeptide wherein said peptide or polypeptide comprises:

- i) SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:77, or one of SEQ ID NO:41 through SEQ ID NO: 74; or
- ii) a peptide having 1 to 10 conservative amino acid substitutions of SEQ ID NO:5, SEQ ID NO:6, or one of SEQ ID NO:41 through SEQ ID NO:74.

50. (new) The method of claim 49, wherein a peptide is administered, and wherein said peptide comprises SEQ ID NO:5, SEQ ID NO:6, or SEQ ID NO:77.

51. (new) The method of claim 49, wherein said peptide or polypeptide is coupled to a terminal protecting group at the N- and/or C- termini.

52. (new) The method of claim 49, wherein said peptide or polypeptide comprises SEQ ID NO:5.

53. (new) The method of claim 49, wherein said peptide or polypeptide is conjugated to a carrier protein.

54. (new) The method of claim 53, wherein said carrier protein is keyhole limpet hemocyanin (KLH), ovalbumin, bovine serum albumin (BSA) or tetanus toxoid.

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55. (new) A method of raising a broadly neutralizing antibody response to HIV comprising:

administering to a mammal a composition including at least two peptides or polypeptides, wherein said peptides or polypeptides comprise SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:3 and SEQ ID NO:6, SEQ ID NO:2 and SEQ ID NO:6, or SEQ ID NO:3 and SEQ ID NO:5.

56. (new) The method of claim 55, wherein peptides or polypeptides form a stable six helix bundle structure.

57. (new) A method of raising a broadly neutralizing antibody response to HIV comprising:

administering to a mammal a composition including at least one conjugate peptides or polypeptides formed from two or more amino acid sequences that comprise:

- i) one or more amino acid sequence SEQ ID NO:2, SEQ ID NO:3, or one of SEQ ID NO:9 through SEQ ID NO:40 or peptides having 1 to 10 conservative amino acid substitutions of each sequence; and
- ii) one or more amino acid sequence SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, or one of SEQ ID NO:41 through SEQ ID NO:74 or a peptide having 1 to 10 conservative amino acid substitutions of each sequence;

wherein,

said one or more sequences (i) and (ii) are alternatively linked to one another via a bond, such as a peptide bond (amide linkage) or by an amino acid linking sequence consisting of about 2 to about 25 amino acids.

58. (new) A method of claim 57, wherein said amino acid linking sequence is of a (GGGS)₃ motif (SEQ ID NO:7).

59. (new) The method of claim 57, wherein sequence a) comprises SEQ ID

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NO:2 or 3 and sequence b) comprises SEQ ID NO:5 or SEQ ID NO:6.

60. (new) The method of claim 59, wherein the sequence of (a) is linked to a sequence of (b) is linked to (a) sequence.

61. (new) The method of claim 59, wherein a sequence of (b) is linked to a sequence of (a) is linked to a sequence of (b).

62. (new) The method of claim 59, wherein said one or more sequences is one of (a) and (b), and wherein said peptides are coupled to a larger carrier protein.